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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/977,693	10/16/2001	Jonathan S. Stamler	Duke 1931	3762

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EXAMINER

LAMBERTSON, DAVID A

ART UNIT PAPER NUMBER

1636

DATE MAILED: 07/13/2004

Please find below and/or attached an Office communication concerning this application or proceeding.

**Office Action Summary**

Application No.

09/977,693

Applicant(s)

STAMLER, JONATHAN S.

Examiner

David A. Lambertson

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-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

**Period for Reply**

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

**Status**

- 1) ☒ Responsive to communication(s) filed on 19 April 2004.
- 2a) ☐ This action is **FINAL**. 2b) ☒ This action is non-final.
- 3) ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

**Disposition of Claims**

- 4) ☒ Claim(s) 1-3, 5-9, 11 and 12 is/are pending in the application.
- 4a) Of the above claim(s) 11 and 12 is/are withdrawn from consideration.
- 5) ☐ Claim(s) \_\_\_\_\_ is/are allowed.
- 6) ☒ Claim(s) 1-3 and 5-9 is/are rejected.
- 7) ☐ Claim(s) \_\_\_\_\_ is/are objected to.
- 8) ☐ Claim(s) \_\_\_\_\_ are subject to restriction and/or election requirement.

**Application Papers**

- 9) ☐ The specification is objected to by the Examiner.
- 10) ☐ The drawing(s) filed on \_\_\_\_\_ is/are: a) ☐ accepted or b) ☐ objected to by the Examiner.  
Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).  
Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).
- 11) ☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

**Priority under 35 U.S.C. § 119**

- 12) ☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).
- a) ☐ All b) ☐ Some \* c) ☐ None of:
1. ☐ Certified copies of the priority documents have been received.
2. ☐ Certified copies of the priority documents have been received in Application No. \_\_\_\_\_.
3. ☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).
- \* See the attached detailed Office action for a list of the certified copies not received.

**Attachment(s)**

- 1) ☒ Notice of References Cited (PTO-892)
- 2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
- 3) ☐ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08)  
Paper No(s)/Mail Date \_\_\_\_\_
- 4) ☐ Interview Summary (PTO-413)  
Paper No(s)/Mail Date. \_\_\_\_\_
- 5) ☐ Notice of Informal Patent Application (PTO-152)
- 6) ☐ Other: \_\_\_\_\_

### **DETAILED ACTION**

Receipt is acknowledged of a reply to the previous Office Action, filed April 19, 2004. Amendments were made to the claims. Specifically, claims 4 and 10 were cancelled.

Claims 1-3, 5-9, 11 and 12 are pending in the instant application. Claims 11 and 12 are withdrawn. Claims 1-3 and 5-9 are under examination in the instant application. Any rejection of record in the previous Office Action, mailed November 18, 2003, that is not addressed in this action has been withdrawn.

Because the previous rejections have been withdrawn, Applicant's arguments with regard to those rejections are moot, and will not be addressed further in this Office Action.

### ***Claim Rejections - 35 USC § 102***

The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

A person shall be entitled to a patent unless –

(a) the invention was known or used by others in this country, or patented or described in a printed publication in this or a foreign country, before the invention thereof by the applicant for a patent.

(b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

It is noted that the following rejections are based on the following interpretation of the claims, particularly regarding the terms "proteomic interaction." It is noted that, in the instant specification (page 4, lines 10-14), the term "proteomic interaction" is defined as representing a change in expression level of a protein, a change in a protein's interaction with another molecule (including other proteins, DNA and RNA) and a change in the activity of a protein.

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Claims 1 and 2 are rejected under 35 U.S.C. 102(b) as being anticipated by Abate *et al.* (*Science* **249**:1157-1161, 1990; see entire document; henceforth Abate).

Abate teaches a method whereby the effects of sulfhydryl modifications are examined with regard to their effects on the dimerization and DNA-binding activities of the Fos and Jun proteins (see for example page 1158, left column, first full paragraph). The interactions between Fos and Jun, and their interaction with DNA, represent “proteomic interactions” as defined by the instant specification. Notably, the effects are measured both in the presence and absence of oxidizing agents, in particular N-ethylmaleimide and diamide (see for example page 1158, paragraph bridging the left and middle columns). The results of the method are presented in Figures 2A-C on page 1159, whereby it is ascertained that the oxidizing agents inhibit the DNA binding activities of Fos and Jun.

Claims 5, 6 and 9 are rejected under 35 U.S.C. 102(b) as being anticipated by Goldberg *et al.* (*Science* **242**:1412-1415, 1988; see entire document; henceforth Goldberg).

Goldberg teaches the determination of protein expression levels for Epo in response to hypoxic (decreased oxygen tension) conditions (see for example Figure 3A-C and the corresponding legend). As per the definition set forth in the instant specification, measuring the expression level of a protein represents a “proteomic interaction.” In particular, the expression levels are measured in response to different oxygen levels, wherein the “control” step is performed under room air conditions, and additional steps are performed at decreased oxygen tensions of 1% oxygen concentration (again see for example Figure 3A-C and the corresponding legend). Epo is known to be involved in the physiological process of red blood cell production,

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and is correlated with a response to the pathophysiological condition of hypoxia, as a result of its induction in response to hypoxic conditions (see for example the Abstract).

Claims 1-3 are rejected under 35 U.S.C. 102(b) as being anticipated by Saitoh *et al.* (*EMBO J* 17: 2596-2606; see entire document; henceforth Saitoh).

Saitoh teaches a method whereby the interaction between apoptosis signal-regulating kinase (ASK1) and thioredoxin (Trx) is examined under normal and simulated redox conditions (see for example the Abstract, page 2599-2600, the section beginning with “Redox status-dependent interaction of Trx and ASK1,” and Figure 6). The interaction between ASK1 and Trx is by definition a “proteomic interaction” given the meaning set forth in the instant specification. Specifically, the interaction between ASK1 and Trx is measured in the absence of a redox agent (controls), as well as in the presence of redox agents such as diamide and hydrogen peroxide (again see for example page 2599-2600, the section beginning with “Redox status-dependent interaction of Trx and ASK1 and Figure 6).

Claims 1-3 are rejected under 35 U.S.C. 102(b) as being anticipated by Nishiyama (*J. Biol. Chem.* 274: 21645-21650; see entire document; henceforth Nishiyama).

Nishiyama teaches a method whereby the yeast two-hybrid system was used to identify the interaction between Trx and several candidate proteins, identifying three different candidate genes (see for example page 21646, right column, last paragraph). Nishiyama then explores the “proteomic interactions” between Trx and one candidate, TBP-2, under redox conditions (see for example page 21647, left column, bottom paragraph and Figure 3). Specifically, Nishiyama

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shows that the interaction between Trx and TBP-2 is inhibited by the presence of the redox agents diamide and hydrogen peroxide (again see for example page 21647, left column, bottom paragraph and Figure 3).

Claims 1-3 and 5-9 are rejected under 35 U.S.C. 102(a) as being anticipated by Ratcliffe *et al.* (WO 00/69908; see entire document; henceforth Ratcliffe).

Ratcliffe teaches a method for assaying the modulation of the interaction between VHL (a protein involved in Von Hippel-Lindau disease) and HIF $\alpha$  (see for example page 3, lines 6-13), wherein the use of variants, fragments and orthologues of both VHL (see for example page 5, lines 7-16) and HIF $\alpha$  (page 6, line 28 to page 7, line 12) is contemplated. A preferred format for performing the assay is via a two-hybrid assay (see for example page 9, line 2 to page 10, line 3). The assays are contemplated as being performed in the presence of 21% oxygen, 5% carbon dioxide and balanced nitrogen levels (room air conditions), and in the presence and absence of the redox modifier hydrogen peroxide (see for example page 3, line 29 to page 4, line 3).

Ratcliffe also teaches that, in addition to the “normoxic” conditions set forth above, “hypoxic” conditions (i.e., decreased oxygen tension) using 0.1% to 1.0% oxygen (see for example page 12, line 14 to page 13, line 3). Presuming the assay was performed at sea level ( $P_{\text{TOTAL}} = 760$  mm Hg), and given the equation for the determination of partial pressure ( $P_{\text{O}_2} = P_{\text{TOTAL}} \times \% \text{O}_2$ ), the range of 0.1% to 1.0% oxygen is equivalent to using partial pressures of 0.76-7.6 mm Hg. This falls within the range set forth in instant claim 8, thereby anticipating the claim.

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*Allowable Subject Matter*

No claims are allowable.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to David A. Lambertson whose telephone number is (571) 272-0771. The examiner can normally be reached on 6:30am to 4pm, Mon.-Fri., first Friday off.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Remy Yucel, Ph.D. can be reached on (571) 272-0781. The fax phone number for the organization where this application or proceeding is assigned is 703-872-9306.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see <http://pair-direct.uspto.gov>. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

David A. Lambertson, Ph.D.  
AU 1636

  
JAMES KETTER  
PRIMARY EXAMINER